

AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning at page 12, line 12, as follows:

The peptide utilized within this embodiment is selected from the group consisting of:  
a flexible linker such as a glycine rich linker such as ~~(SG<sub>4</sub>)<sub>n</sub>~~ (SG<sub>4</sub>)<sub>n</sub> (SEQ ID NO: 107) or the  
sequence SG<sub>4</sub>CG<sub>4</sub> (residues 3-12 of SEQ ID NO: 39),

human calmodulin (SEQ ID NO: 46, the DNA encoding SEQ ID NO: 46 is SEQ ID  
NO: 56), and

hexahistidine (SEQ ID NO: 108) binding single chain variable fragment (Grütter  
M.G., 2002) consisting of:

- (i) Anti-His Tag Antibody 3D5 Variable Heavy Chain (SEQ ID NO: 47)
- (ii) Linker (SEQ ID NO: 48)
- (iii) Anti-His Tag Antibody 3D5 Variable Light Chain (SEQ ID NO: 49).

Please amend the paragraph beginning at page 17, line 24, as follows:

The peptide *m*, SG<sub>4</sub>CG<sub>4</sub> (residues 3-12 of SEQ ID NO: 39), at the N-terminus of the  
mature fusion protein, was found to increase the display of *B. pertussis* cyclase-polymerase  
fusion on phage, by 100-fold for signal sequence 17 and by 10-fold for *pelB*. For this fusion,  
the worst display ratios are significantly improved with peptide *m*. Display of *B. pertussis*  
cyclase on phage was high in all cases, such that a marginal improvement due to the *m*  
peptide was found for signal sequence 17, and improvement within the limits of experimental  
error for *pelB*. Concerning the *E. coli* cyclase protein, peptide *m* decreases the latter's display  
by a factor of 30 to 40. For the *E. coli* cyclase-polymerase fusion, peptide *m* showed no

significant effect with the signal sequence ~~pelB~~ peIB and a small improvement with signal sequence 17.

Please amend the paragraph beginning at page 19, line 3, as follows:

In the work reported here, the present inventors investigated the display of adenylate cyclases from *B. pertussis* and from *E. coli* on filamentous phage, and the display of two independent enzymes, an adenylate cyclase and the Taq DNA polymerase I Stoffel fragment. The Stoffel fragment (Lawyer, F.C., Stoffel, S., Saiki, R.K., et al., 1989) could be used as a tool to establish an ~~in-vitro~~ in vitro selection for cyclase activity as follows: the polymerase domain may serve as an anchor of the substrate ATP on phage through double-stranded DNA used as a linker with a high affinity for the fusion protein. Another approach to cross-linking substrate and phage involves introduction of the thiol group of a cysteine residue within peptide *m* (SG<sub>4</sub>CG<sub>4</sub>) (residues 3-12 of SEQ ID NO: 39), at the N-terminus of the mature fusion protein and at the C-terminus of the fusion protein's signal sequence (Jestin et al., 1999).

Please amend the paragraph beginning at page 19, line 14, as follows:

The signal sequences 17, 110, and 112, used in the present inventors' study had been selected from large libraries of ~~pelB~~ peIB mutants for optimal display of the Stoffel fragment-p3 protein fused to the peptide *m* (Jestin et al., 2001). It was therefore important to further investigate which sequence context was essential for selection of these signal sequences, either the short peptide *m* or the entire gene. Interestingly, the present inventors found that the presence or the absence of this short peptide, SG<sub>4</sub>CG<sub>4</sub> (residues 3-12 of SEQ ID NO: 39), can

yield up to 100-fold increases in the display of a fusion protein on filamentous phage. This strong effect was observed for the *B. pertussis* cyclase-Stoffel-p3 fusion as well as for the *E. coli* cyclase-p3 fusion in the case of the signal sequence 17 (Table 2). Of further note is that the signal sequences 17 and 112, yield generally better levels of protein display on phage than does ~~pelB~~ *pelB* (Figure 3). This improved display of proteins might be ascribed to the different targeting modes of the signal sequences. These selected signal sequences that improve the display of proteins on phage should therefore be useful in other systems.

Please amend the paragraph beginning at page 21, line 27, as follows:

Residues 1-12 of SEQ ID NO: 26 correspond to SEQ ID NO: 39, which contain 2 residues from the signal sequence (MetAla) and 10 residues (SerGly<sub>4</sub>CysGly<sub>4</sub>) (residues 3-12 of SEQ ID NO: 39) corresponding to a linker that had been introduced at N-terminus of the mature fusion protein on phage so as to introduce a cysteine residue that might be important for substrate cross-linking on phage. Further residues 556-562 correspond to residues 1-7 of SEQ ID NO: 40, which is the resultant sequence following thrombin cleavage of the sequence of SEQ ID NO: 40. It should also be understood that the present invention embraces sequences corresponding to residues 13-555 of SEQ ID NO: 26 as defined herein, as well as sequences in which the N-terminus and C-terminus contain signal sequences, linker sequences, purification tags, and/or fusion constructs.

Beginning on new page 76, please insert the attached abstract.

Please delete the originally filed Sequence Listing.

Docket No. 295295US0XPCT

Application Serial No. 10/590,810

Preliminary Amendment and Response to Notification to Comply dated May 3, 2007

Beginning on new page 77, please insert the attached Substitute Sequence Listing.